

Citation for published version:

Agostinho Hernandez, B, Gill, R & Gheduzzi, S 2020, 'Material property calibration is more important than element size and number of different materials on the finite element modelling of vertebral bodies: A Taguchi study', *Medical Engineering & Physics* , vol. 84, pp. 68-74. <https://doi.org/10.1016/j.medengphy.2020.07.009>

DOI:

[10.1016/j.medengphy.2020.07.009](https://doi.org/10.1016/j.medengphy.2020.07.009)

Publication date:

2020

Document Version

Peer reviewed version

[Link to publication](#)

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Material property calibration is more important than element size and number of different materials on the finite element modelling of vertebral bodies. A Taguchi study.

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Abstract

Finite element (FE) modelling of a vertebral body (VB) is considered challenging due to the many parameters involved such as element size and type, and material properties. Previous studies have reported how these parameters affect the mechanical behaviour of a VB model; however, most studies just compared results without any specific statistical tool to quantify their influence. The Taguchi Method (TM) has been successfully used in manufacturing and biomechanics to evaluate process parameters and to determine optimum set-up conditions. This study aimed to evaluate the influence of the main finite element modelling parameters on the mechanical behaviour of a VB model using the Taguchi Method. A FE model was developed based on a C2 juvenile porcine vertebral body and three of the most commonly used modelling parameters were evaluated using TM in terms of change in the predicted stiffness in comparison to experimental values: element size, number of different material properties for VB (based on grey-scale bins) and calibration factor for grey-scale to density to Young's Modulus equation. The influence of the combined factors was also assessed. The Taguchi analysis showed that the three factors are independent. The calibration factor is the main contributor, accounting for 97% of the predicted stiffness, with the value of 0.03 most closely aligning the numerical and experimental results. element size accounted for 2% of the predicted stiffness, with 0.75 mm being the optimal, while the number of grey-scale bins influenced the results by less than 1%. Our findings indicate that the calibration factor is the main modelling parameter, with the element size and number of bins accounting for less than 3% of the predicted stiffness. Therefore, calibration of material properties should be done based on a large number of samples to ensure reliable results.

Keywords: Taguchi Method, Finite Element method, vertebral bodies.

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1. Introduction

Finite element (FE) models have been widely applied in orthopaedic research to evaluate spine injuries and to characterise the mechanical behaviour of vertebral bodies and intervertebral discs (Brown, 2004; Wijayathunga et al., 2008; Cronin, 2014). However, their accuracy is highly dependant on several factors, such as material properties, boundary conditions, load application and element size (Kopperdahl et al., 2002; Jones and Wilcox, 2007; Wijayathunga et al., 2008). As a consequence, several studies have explored the influence of these modelling factors and how they individually affect model's prediction capabilities (Keyak and Skinner, 1992; Crawford et al., 2003b; Brown, 2004; Jones and Wilcox, 2007; Zander et al., 2016).

The most frequent analysed factor is the element size (Keyak and Skinner, 1992; Crawford et al., 2003b; Yeni et al., 2005; Jones and Wilcox, 2007; Guldberg et al., 2008). According to Jones and Wilcox (2007), an ideal element size is a compromise between accuracy, in the description of geometrical and material features, and computational costs. Nevertheless, there is still uncertainty to what the ideal element size is. For example, a study conducted by Crawford et al. (2003b) evaluated how the element size and image resolution affects the prediction of vertebral stiffness. They found that element size does not affect the model stiffness, and it has a similar influence as specimens anatomy variability. Another study, on the other hand, highlighted that there is a significant difference in predicted vertebral stiffness for larger element sizes (more than 3 mm), especially for specimen-specific models (Jones and Wilcox, 2007).

Another factor that has not been fully evaluated is the relationship between material properties and density. The use of specimen-specific properties based on grey-scale to Young's Modulus equations have increased the accuracy of the models and allowed an element-based material definition (Wilcox, 2007). In other words, a body would have several groups (or bins) of material according to its density distribution. However, the precise number of different materials required to describe the trabecular structure is still unknown. In one of the few studies covering this issue, Giambini et al. (2015) evaluated the influence of the number of different materials on the predicted stiffness using QCT/FE models of vertebral bodies. They found that for 8, 18 and 50 different materials, the difference relative to the experimental results were 21%, 6% and 1%, respectively.

An additional problem that has risen with specimen-specific FE models, and it still has not

31 been addressed, is the influence of the calibration factor of grey-scale to Young's Modulus
32 equations. The literature is populated with several different equations, and they widely vary
33 in terms of density range, experimental technique and formulation type (i.e. linear or power
34 laws) (Helgason et al., 2008). In order to overcome these issues, some studies make the use of a
35 coefficient, which re-calibrates these equations for their sample density and testing conditions
36 (Wijayathunga et al., 2008; Mengoni et al., 2016).

37 Finally, the majority of studies available in the literature only compared the results from a re-
38 latively small set of simulations, without using any specific statistical tool to quantify their
39 influence, and used the simplistic approach of testing one factor at time. Also, the interactions
40 between factors, i.e. if one factor affects the other, have remained unexplored. The Taguchi
41 Method has been successfully used in engineering to estimate the effect of factors and their in-
42 teractions on a desired outcome (Taguchi, 1986; Belavendram, 1995; Dar et al., 2002). Instead of
43 investigating all possible combinations to analyse the influence of a specific set of parameters,
44 which can be time-consuming, Taguchi uses orthogonal arrays, and a relatively small and spe-
45 cific combination of parameters to achieve the same results, reducing time costs and increas-
46 ing productivity. The aim of this study was, therefore, to quantify the influence of the main
47 well-defined modelling factors, element size, calibration factor and number of bands (bins) of
48 materials, on the prediction of the stiffness of a vertebral body FE model using the Taguchi
49 Method.

50 **2. Materials and Methods**

51 *2.1. Taguchi Experiments*

52 In order to set a Taguchi analysis, it is firstly necessary to understand the basic concepts of it.
53 Any studied parameter is called factor and any value assigned to it is named level (Taguchi,
54 1986; Belavendram, 1995). For example, if a factor has two levels, it means that the parameter
55 has two possible values. For this study, three factors were initially chosen based on literature:
56 grey-scale calibration factor, element size and number of grey-scale bins (or materials). In order
57 to explore the full potential of the method, three extra factors were added to account for the
58 interactions between the three primary factors, i.e. if the change in one affects the other. A total
59 of six factors were then analysed, and there were labelled as A, B and C for grey-scale factor,

60 element size and number of grey-scale bins, respectively, and as AxB, AxC and BxC for the
61 interactions. Each level was assumed to be linear and it was labelled as one or two, Table 1.

62 After setting the factors and their levels, it is necessary to select an orthogonal array with
63 enough iteration spaces. An orthogonal array is a table that contains all necessary combin-
64 ations of the factors. Its size varies according to the number of factors and levels, and they
65 are available elsewhere (Taguchi, 1986; Belavendram, 1995). Each combination of factors is la-
66 belled as an experiment. For example, if four experiments are run, it means that four different
67 combinations of factors were tested. For the current study, an orthogonal array $L_8(2^7)$ was se-
68 lected, which consists of eight experiments (or combinations), and this can analyse up to seven
69 factors, with two levels each, Table 2 (Taguchi, 1986). The results were evaluated in terms of
70 the stiffness of the vertebral body, i.e. how much the factors changed the predicted stiffness
71 of the finite element model compared to the experimentally measured stiffness. In order to
72 complement Taguchi analyses, an Analysis of Variance (ANOVA) was also conducted.

Table 1: Analysed factors and their levels.

Factor	Levels		
FactGS	A	0.1	0.03
Mesh	B	1.25	0.75
Bins	C	50	20
		1	2

Table 2: $L_8(2^7)$ Orthogonal Array for Taguchi Experiments.

Experiment	Factors $L_8(2^7)$						
	1	2	3	4	5	6	7
	A	B	AxB	C	AxC	BxC	e
1	1	1	1	1	1	1	1
2	1	1	1	2	2	2	2
3	1	2	2	1	1	2	2
4	1	2	2	2	2	1	1
5	2	1	2	1	2	1	2
6	2	1	2	2	1	2	1
7	2	2	1	1	2	2	1
8	2	2	1	2	1	1	2

73 2.2. Experimental Procedure for comparison

74 A compression-load experiment was performed in order to acquire data for comparison. A
75 juvenile porcine cervical spine (ageing between 8 and 12 months) was acquired from a local
76 abattoir, dissected and a C2 vertebral body was potted separately in polymethyl methacrylate

77 (PMMA) bone cement (Simplex, Stryker Corporation, USA), Figure 1a. This specimen was
 78 μ CT scanned (Nikon XTH225ST CT Scanner - Nikon Metrology UK, Hertfordshire, UK) and an
 79 image file with a voxel size of 0.10 mm was obtained.

80 The sample was then positioned on a material testing machine (Instron 5967, High Wycombe,
 81 UK), and a compressive vertical load up to 10 kN at 1000 N min^{-1} was applied to the sample's
 82 top surface. In order to avoid any local deformation on the cement and to certify that a uniform
 83 load would be applied, an aluminium plate was placed between the cement and the actuator
 84 of the test machine, Figure 1b. The experimental stiffness was measured in the most linear part
 85 of the load *versus* displacement curve generated from the materials testing machine data and
 86 processed by Matlab (v.R2016b, MathWorks Inc, MA, USA).

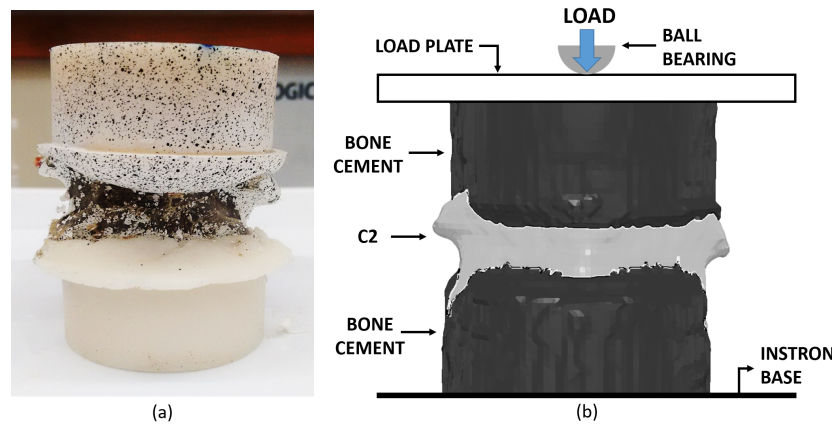


Figure 1: (a) Potted C2 vertebral body. (b) Testing set-up. Load was applied at the centre of the vertebral body.

87 2.3. Numerical Model

88 A numerical model was created from the μ CT images (v.2017, Simpleware ScanIP, Synopsys
 89 Inc, California, USA), Figure 2a. This model comprised the cranial and caudal cement pots, the
 90 C2 vertebral body, cartilage (remaining from dissection) and the aluminium plate. The element
 91 types chosen for this study were a mixture of hexahedrons, to represent the internal trabecular
 92 structure, and tetrahedrons, to represent the external surface (Jones and Wilcox, 2007; Chevalier
 93 et al., 2008; Wijayathunga et al., 2008; Robson Brown et al., 2014; Pahr et al., 2014).

94 Two different mesh sizes were created, one with element length of 1.25 mm and the other with
 95 0.75 mm. The first value is commonly found in literature as default element size (Jones and
 96 Wilcox, 2007; Crawford et al., 2003b; Jones and Wilcox, 2007; Zeinali et al., 2010; Unnikrishnan

and Morgan, 2011; Robson Brown et al., 2014). The latter number was the minimum element size for which simulations could be generated within an acceptable time frame. The original model, with a resolution of 0.10 mm, was then resampled to the required sizes. A total of eight models were created, according to the required combination of parameters, Table 2.

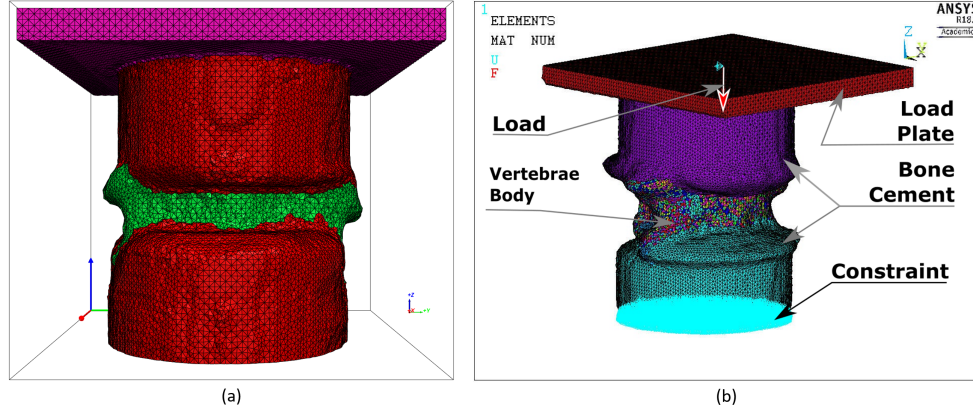


Figure 2: Numerical model of a C2 vertebral body. (a) At Simpleware ScanIP software; (b) Boundary conditions at ANSYS Mechanical APDL v18.1.

The material properties for the bone cement and the aluminium plate were set as isotropic and linear. The cartilage was set as hyper-elastic (Rohlmann et al., 2007). The properties for the cartilage and plate were based on literature data and the cement on a custom materials test, Table 3.

Table 3: Material properties applied to the FE model.

Body	Type	Elastic Parameter [MPa]	Poisson	Reference
Cartilage	Hyperelastic	$C_{10} = 0.3448, D_1 = 0.3$	-	(Rohlmann et al., 2007)
	Neo-Hookean			
Cement	Isotropic	$E = 1177$	0.3	Custom testing
Aluminum Plate	Isotropic	$E = 70000$	0.35	(McCormack et al., 1999)

The number of bins (or the number of different materials) for the vertebral body was based on the common values found in literature: 50 or 20 groups of different materials (Jones and Wilcox, 2007; Giambini et al., 2015). These material properties were based on the grey-scale information acquired using calibration phantoms and on the equation provided elsewhere (Kopperdahl et al., 2002):

$$E_{zz} = 2980 \cdot \rho_{App}^{1.05} \quad (1)$$

where ρ_{App} is the apparent density, in g cm^{-3} , and E is Young's Modulus, in MPa. The above equation was formulated based on elderly and human cervical vertebral bodies and, therefore, it needed to be adapted, i.e. rescaled, for juvenile porcine specimens using a multiplying grey-scale factor previously mentioned. The values for the factor, Table 1, were 0.1 (10% of the original value) and 0.03 (the lowest limit which the mean Young's modulus was in the range of the acceptable values (Teo et al., 2006)). The material properties for the vertebral body were considered to be orthotropic, Equations 2 (Crawford et al., 2003a,b; Zeinali et al., 2010; Ayturk and Puttlitz, 2011; Unnikrishnan and Morgan, 2011; Unnikrishnan et al., 2013).

$$E_{xx} = 0.333 \cdot E_{zz} \quad (2)$$

$$E_{yy} = 0.333 \cdot E_{zz}$$

$$G_{xy} = 0.121 \cdot E_{zz}$$

$$G_{xz} = 0.157 \cdot E_{zz}$$

$$G_{yz} = 0.157 \cdot E_{zz}$$

$$\nu_{xy} = 0.381$$

$$\nu_{xz} = 0.104$$

$$\nu_{yz} = 0.104$$

The models were then exported from ScanIP to Ansys Mechanical APDL 18.1 (Ansys Inc., Pennsylvania, USA), where the boundary conditions, constraints and load application point were applied to replicate the *in vitro* test, Figure 2b. The predicted stiffness of each model was estimated from the calculated load *versus* displacement curve. The load was acquired from the reaction forces, and the displacement was obtained from a node at the top surface of the top cement housing, directly below the load application point; a similar location to that which the testing machine applied the load.

3. Results

3.1. Experimental Results

The data acquired from the material testing machine were plotted in a load *versus* displacement curve and the stiffness was measured based on the most linear part. In this case, it was between 2 kN and 4 kN of the load values, giving a stiffness value of 2854 N mm^{-1} , Figure 3.

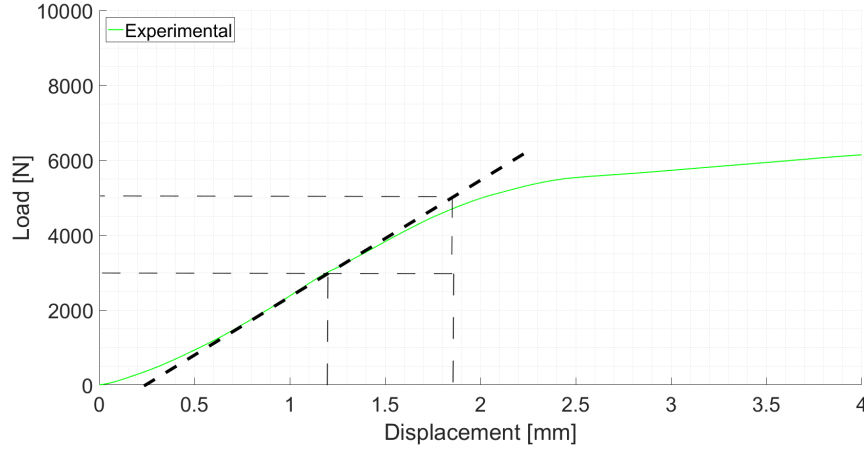


Figure 3: Experimental results of C2 vertebral body.

3.2. Numerical and Taguchi Results

Each model generated a load *versus* displacement curve from which stiffness also was estimated between load values of 2 kN and 4 kN, Figure 4 and Table 4. The models with the greater grey-scale factor presented the highest stiffness values, with the model with a element size of 1.25 mm and 50 bins of materials, Experiment 2, having the highest value, 6726 N mm^{-1} . In contrast, the models with a grey-scale factor of 0.03 had the lowest values of stiffness, with the model with a element size of 0.75 mm and 20 material bins, Experiment 7, having the lowest, 2521 N mm^{-1} . The closest values of predicted stiffness to the experimental were from models 5 and 6, 2751 N mm^{-1} and 2823 N mm^{-1} , respectively, with both having grey-scale factor of 0.03 and element size of 1.25 mm, but 50 and 20 material bins, respectively.

The Analyse of Variance (ANOVA) confirmed what was indicated in the Taguchi experiments (Table 5). Grey-scale factor was the main contributor of the predicted stiffness, accounting for 97% of it, with the value of 0.03 most closely aligning numerical and experimental results. element size accounted for 2% of the predicted stiffness. Due to the low influence on the prediction

Table 4: Results for the Taguchi Experiments

Experiment	Factors $L_8(2^7)$							Calculated Stiffness
	1 A	2 B	3 AxB	4 C	5 AxC	6 BxC	7 e	
1	1	1	1	1	1	1	1	6607
2	1	1	1	2	2	2	2	6726
3	1	2	2	1	1	2	2	5849
4	1	2	2	2	2	1	1	5962
5	2	1	2	1	2	1	2	2751
6	2	1	2	2	1	2	1	2823
7	2	2	1	1	2	2	1	2521
8	2	2	1	2	1	1	2	2561
Average								4475

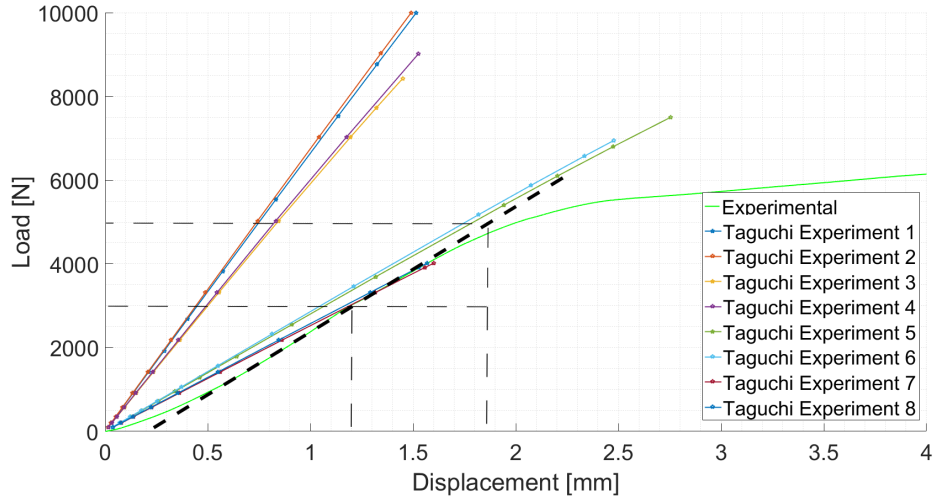


Figure 4: Stiffness predictions from the eight numerical models.

151 of stiffness, factors C, AxC and BxC were excluded from the analysis after a preliminary ana-
 152 lysis with ANOVA.

153 The response graph, Figure 5, also indicates that the grey-scale factor was the main variable,
 154 as the gradient of the curve between levels one and two was the highest among the variables,
 155 followed by element size. The results also showed that these three factors are independent. In
 156 other words, one factor does not have an affect on the other, as the interaction between them
 157 were excluded from ANOVA, and the contribution of the interaction between A and B was only
 158 0.5%. This is also confirmed by the response graph, as the curves AxB did not cross each other
 159 (Taguchi, 1986).

Table 5: Analysis of Variance (ANOVA) of the main contributors for numerical stiffness, where Sq is the Sum of Squares, ν is DoF of the variable, Mq is the Mean Sum of Squares, F-Ratio is a hypothesis test, Sq' is the Corrected Sum of Squares after pooling, and ρ is the contribution percentage. St is the total sum.

Source	Pool	Sq	ν	Mq	F-Ratio	Sq'	ρ %
A		26231248	1	26231248	6236	26227043	97
B		507427	1	507427	121	503222	1.9
AxB		132716	1	132716	32	128510	0.5
C	Y	14740	1	14740	3.50	10535	0.039
AxC	Y	1818.04	1	1818	0.43	-2388	-0.009
BxC	Y	180.50	1	180.50	0.04	-4025	-0.015
e		84.50	0	-	-	-	-
Error	Y	84.50	1	84.50	1	84.50	0.0003
Pooled Error		16823.49	4	4205.87	1	29441.10	0.11
St		26888215.20	7	3841173.60		26888215.20	100

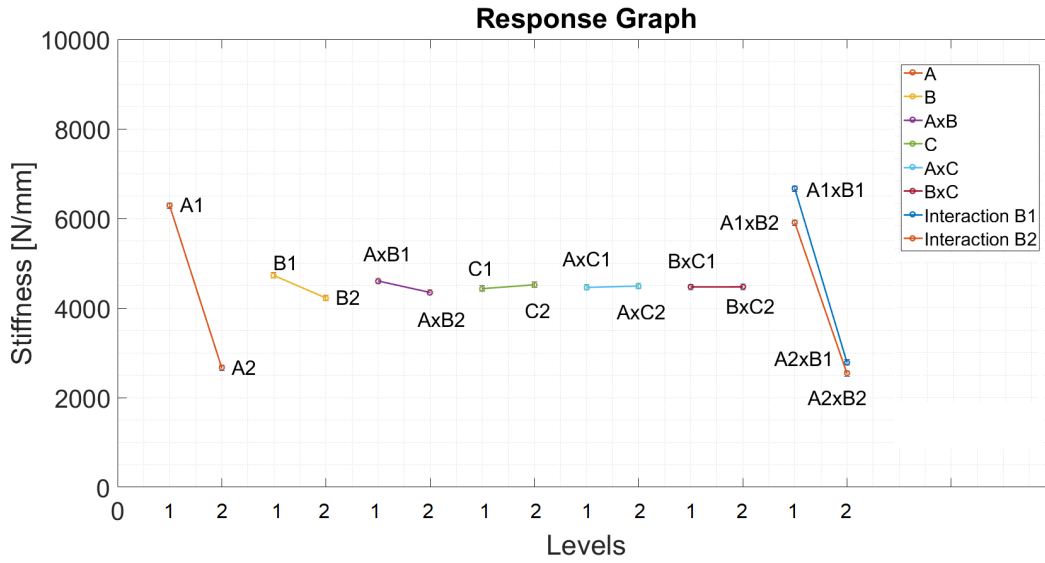


Figure 5: Response graph from ANOVA. As the gradient of the curve between levels one and two was the highest among the variables, grey-scale factor is the main variable, followed by element size. The results also showed that these three factors are independent.

4. Discussion

Finite element modelling of biomechanical structures is a challenging process due to the many factors that can affect the results (Jones and Wilcox, 2008). This study aimed to evaluate the main variables commonly presented in FE modelling of vertebral bodies - grey-scale factor, element size and number of material bands, and how they would affect the predicted stiffness. A better understanding of the modelling process and its variables will save time and reduce overall computational costs as fewer simulations are necessary to build and to calibrate a model. However, differently from other studies, this work did not focus solely on a direct comparison

168 between results, but also on quantifying the influence of variables using a statistical tool.

169 Taguchi's Method is a powerful statistical tool that, combined with ANOVA, allows the quan-
170 tification of a parameter's influence in an outcome. Traditional methods use the direct com-
171 parison approach, in which one variable is changed at a time, resulting in a large number of
172 experiments or simulations (Lee and Zhang, 2005). Taguchi, on the other hand, uses an ortho-
173 gonal array approach to decrease the number of possible combinations and speeding up the
174 analysis process (Belavendram, 1995). This method was already used to analyse geometrical
175 features of dental implants (Dar et al., 2002), on monolimb design (Lee and Zhang, 2005) and
176 on intervertebral disc modelling parameters analysis (Cappetti et al., 2016), but was not previ-
177 ously applied on vertebral body FE models.

178 The first variable, grey-scale factor, was found to be the main contributor for vertebral stiffness.
179 Recent FE models have used greyscale to set the material properties according to the local dens-
180 ity (Tyndyk et al., 2007; Gefen, 2011; Jackman et al., 2016; Mengoni et al., 2016). This approach
181 accounts for differences in density, trabecular structure and orientation inside a vertebral body.
182 Several relationships between Young's Modulus and density are available elsewhere (Morgan
183 et al., 2003; Teo et al., 2006; Helgason et al., 2008). Such equations were developed based on eld-
184 erly human vertebral bodies, which usually are characterised by low-density trabecular bone.
185 Some studies, on the other hand, tried to adapt these equations using a downgrading factor, as
186 they used porcine as testing samples (which are denser than humans vertebral bodies) (Jones
187 and Wilcox, 2007; Wilcox, 2007; Wijayathunga et al., 2008). A high dependency of stiffness on
188 the rescaling factor was expected, and it suggests that the calibration has to be done based on a
189 large number of samples, to ensure that no other external factor is affecting the results.

190 In contrast to the grey-scale factor, differences in element size and the number of material bins
191 (or bands), combined, just changed the overall stiffness by 3%. Element size effect has been
192 widely studied in recent years and highlighted as one of the main parameters in a FE model
193 (Keyak and Skinner, 1992; Yeni et al., 2005; Jones and Wilcox, 2007; Hosseini et al., 2014). The
194 majority of the studies reported good convergence for models with element size up to 1.5 mm,
195 with 1.0 mm being the most common option (Jones and Wilcox, 2007). The current study used
196 element sizes of 1.25 mm and 0.75 mm, thus within the reported range. This could explain the
197 low effect of element size in the stiffness as this study already used optimum values.

198 The influence of the number of material bands, differently from element size, has not been well
199 explored (Giambini et al., 2015). Gefen (2011) conducted a study to understand the influence of
200 the number of Young's Modulus values required to represent the vertebral bone. They found
201 that a change in the number of different materials, from two to five bands, did not affected the
202 stiffness significantly. However, another study found that between 42 and 50 different material
203 bands would be necessary to completely describe the cancellous bone structure (Giambini et al.,
204 2015). In this study, 20 and 50 bands were chosen in order to explore a wider range and to
205 include the optimum value found by Giambini et al. (2015). The changing on the number of
206 material bands showed no influence on the stiffness, and it was excluded from the analysis
207 by the ANOVA. This can be also confirmed by analysing Table 4. A change of bands, from
208 Experiment 1 to 2, did not altered significantly the stiffness, from 6607 N mm^{-1} to 6726 N mm^{-1} .
209 In addition to element size, another limitation of this study was the adoption of only two levels
210 and three parameters. It is widely known that several parameters can affect the numerical res-
211 ults. Also, two levels should be used when the variable behaves linearly (Belavendram, 1995),
212 which might not be true for finite modelling of vertebral bodies. However, the introduction
213 of more levels and variables would increase the size and complexity of the orthogonal array
214 and this study aimed to illustrate how a statistical tool could be used to optimise the modelling
215 process of vertebral body models. Further studies are still necessary to explore the combination
216 of more factors and multiple levels in order to set a clear picture of the modelling variables.

217 5. Conclusion

218 This study applied the Taguchi Method to evaluate the influence of the main modelling para-
219 meters on the accuracy of finite element models of vertebral bodies. Grey-scale factor, element
220 size and number of material bands were assessed. Grey-scale factor was the main contributor
221 to the predicted vertebral stiffness, and Taguchi Method was shown to be an efficient statistical
222 tool to quantify the influence of each parameter.

223 Conflict of interest

224 The authors do not have any conflict of interest.

225 Acknowledgement

226 We gratefully acknowledge the support of the Brazilian Government and CAPES for a PhD
227 scholarship (Process n° 99999.001603/2015-09).

228 References

- 229 Ayturk, U. M., Puttlitz, C. M., 2011. Parametric convergence sensitivity and validation of a finite element
230 model of the human lumbar spine. *Computer methods in biomechanics and biomedical engineering*
231 14 (March 2015), 695–705.
- 232 Belavendram, N., 1995. The Design Process. In: Hall, P. (Ed.), *Quality by design*, 1st Edition. Prentice
233 Hall, Ch. Chapter 2.
- 234 Brown, T. D., 2004. Finite element modeling in musculoskeletal biomechanics. *Journal of Applied Bio-*
235 *mechanics* 20 (4), 336–366.
- 236 Cappetti, N., Naddeo, A., Naddeo, F., Solitro, G. F., 2016. Finite elements/Taguchi method based pro-
237 cedure for the identification of the geometrical parameters significantly affecting the biomechanical
238 behavior of a lumbar disc. *Computer Methods in Biomechanics and Biomedical Engineering* 19 (12),
239 1278–1285.
- 240 Chevalier, Y., Charlebois, M., Pahra, D., Varga, P., Heini, P., Schneider, E., Zysset, P., 2008. A patient-
241 specific finite element methodology to predict damage accumulation in vertebral bodies under axial
242 compression, sagittal flexion and combined loads. *Computer methods in biomechanics and biomed-*
243 *ical engineering* 11 (5), 477–487.
- 244 Crawford, R. P., Cann, C. E., Keaveny, T. M., 2003a. Finite element models predict in vitro vertebral body
245 compressive strength better than quantitative computed tomography. *Bone* 33 (4), 744–750.
- 246 Crawford, R. P., Rosenberg, W. S., Keaveny, T. M., 2003b. Quantitative Computed Tomography-Based
247 Finite Element Models of the Human Lumbar Vertebral Body: Effect of Element Size on Stiffness,
248 Damage, and Fracture Strength Predictions. *Journal of Biomechanical Engineering* 125 (4), 434.
- 249 Cronin, D. S., 2014. Finite element modeling of potential cervical spine pain sources in neutral position
250 low speed rear impact. *Journal of the Mechanical Behavior of Biomedical Materials* 33 (1), 55–66.
- 251 Dar, F. H., Meakin, J. R., Aspden, R. M., 2002. Statistical methods in finite element analysis. *Journal of*
252 *Biomechanics* 35 (9), 1155–1161.
- 253 Gefen, A., 2011. *Patient-Specific Modeling in Tomorrow’s Medicine*. Springer.
- 254 Giambini, H., Qin, X., Dragomir-Daescu, D., An, K.-N., Nassr, A., 2015. Specimen-specific vertebral
255 fracture modeling: a feasibility study using the extended finite element method. *Medical & Biological*
256 *Engineering & Computing* 54 (4), 583–593.
- 257 Guldberg, R. E., Hollister, S. J., Charras, G. T., 2008. The Accuracy of Digital Image-Based Finite Element
258 Models. *Journal of Biomechanical Engineering* 120 (2), 289.
- 259 Helgason, B., Perilli, E., Schileo, E., Taddei, F., Brynjólfsson, S., Viceconti, M., 2008. Mathematical rela-
260 tionships between bone density and mechanical properties: A literature review. *Clinical Biomechanics*
261 23 (2), 135–146.

262 Hosseini, H. S., Clouthier, A. L., Zysset, P. K., 2014. Experimental validation of finite element analysis
263 of human vertebral collapse under large compressive strains. *Journal of biomechanical engineering*
264 136 (4), 041006.

265 Jackman, T. M., DelMonaco, A. M., Morgan, E. F., 2016. Accuracy of finite element analyses of CT scans
266 in predictions of vertebral failure patterns under axial compression and anterior flexion. *Journal of*
267 *Biomechanics* 49 (2), 267–275.

268 Jones, A. C., Wilcox, R. K., 2007. Assessment of Factors Influencing Finite Element Vertebral Model
269 Predictions. *Convergence* 129 (December), 2–7.

270 Jones, A. C., Wilcox, R. K., 2008. Finite element analysis of the spine: Towards a framework of verifica-
271 tion, validation and sensitivity analysis. *Medical Engineering and Physics* 30 (10), 1287–1304.

272 Keyak, J. H., Skinner, H. B., 1992. Three-dimensional finite element modelling of bone: effects of element
273 size. *Journal of Biomedical Engineering* 14 (6), 483–489.

274 Kopperdahl, D., Morgan, E., Keaveny, T., 2002. Quantitative computed tomography estimates of the
275 mechanical properties of human vertebral trabecular bone. *J Orthop Res* 20, 801–805.

276 Lee, W. C., Zhang, M., 2005. Design of monolimb using finite element modelling and statistics-based
277 Taguchi method. *Clinical Biomechanics* 20 (7), 759–766.

278 McCormack, B. A. O., Prendergast, P. J., O'Dwyer, B., 1999. Fatigue of cemented hip replacements under
279 torsional loads. *Fatigue and Fracture of Engineering Materials and Structures* 22 (1), 33–40.

280 Mengoni, M., Vasiljeva, K., Jones, A. C., Tarsuslugil, S. M., Wilcox, R. K., 2016. Subject-specific multi-
281 validation of a finite element model of ovine cervical functional spinal units. *Journal of Biomechanics*
282 49 (2), 259–266.

283 Morgan, E. F., Bayraktar, H. H., Keaveny, T. M., 2003. Trabecular bone modulus-density relationships
284 depend on anatomic site. *Journal of Biomechanics* 36 (7), 897–904.

285 Pahr, D. H., Schwiedrzik, J., Dall'Ara, E., Zysset, P. K., 2014. Clinical versus pre-clinical FE models for
286 vertebral body strength predictions. *Journal of the Mechanical Behavior of Biomedical Materials* 33 (1),
287 76–83.

288 Robson Brown, K., Tarsuslugil, S., Wijayathunga, V. N., Wilcox, R. K., 2014. Comparative finite-element
289 analysis: a single computational modelling method can estimate the mechanical properties of porcine
290 and human vertebrae. *Journal of the Royal Society, Interface / the Royal Society* 11 (95), 20140186.

291 Rohlmann, A., Burra, N. K., Zander, T., Bergmann, G., 2007. Comparison of the effects of bilateral pos-
292 terior dynamic and rigid fixation devices on the loads in the lumbar spine: A finite element analysis.
293 *European Spine Journal* 16 (8), 1223–1231.

294 Taguchi, G., 1986. *Introduction to quality engineering: designing quality into products and processes.*
295 Tokyo: Asian Productivity Organization.

296 Teo, J. C. M., Si-Hoe, K. M., Keh, J. E. L., Teoh, S. H., 2006. Relationship between CT intensity, micro-
297 architecture and mechanical properties of porcine vertebral cancellous bone. *Clinical Biomechanics*
298 21 (3), 235–244.

299 Tyndyk, M. A., Barron, V., McHugh, P. E., Mahoney, D., 2007. Generation of a finite element model of the
300 thoracolumbar spine. *Acta of Bioengineering and Biomechanics* 9 (1), 35–46.

301 Unnikrishnan, G. U., Barest, G. D., Berry, D. B., Hussein, A. I., Morgan, E. F., 2013. Effect of specimen-
302 specific anisotropic material properties in quantitative computed tomography-based finite element
303 analysis of the vertebra. *Journal of biomechanical engineering* 135 (10), 101007–11.

304 Unnikrishnan, G. U., Morgan, E. F., 2011. A new material mapping procedure for quantitative computed
305 tomography-based, continuum finite element analyses of the vertebra. *Journal of biomechanical en-
306 gineering* 133 (7), 071001.

307 Wijayathunga, V. N., Jones, A. C., Oakland, R. J., Furtado, N. R., Hall, R. M., Wilcox, R. K., 2008. Develop-
308 ment of specimen-specific finite element models of human vertebrae for the analysis of vertebroplasty.
309 *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*
310 222 (2), 221–228.

311 Wilcox, R. K., 2007. The influence of material property and morphological parameters on specimen-
312 specific finite element models of porcine vertebral bodies. *Journal of Biomechanics* 40 (3), 669–673.

313 Yeni, Y. N., Christopherson, G. T., Neil Dong, X., Kim, D., Fyhrie, D., 2005. Effect of Microcomputed
314 Tomography Voxel Size on the Finite Element Model Accuracy for Human Cancellous Bone. *Journal
315 of Biomechanical Engineering* 127 (1), 1.

316 Zander, T., Dreischarf, M., Timm, A.-K., Baumann, W. W., Schmidt, H., 2016. Impact of material and mor-
317 phological parameters on the mechanical response of the lumbar spine — A finite element sensitivity
318 study. *Journal of Biomechanics*, 10–15.

319 Zeinali, A., Hashemi, B., Akhlaghpour, S., 2010. Noninvasive prediction of vertebral body compressive
320 strength using nonlinear finite element method and an image based technique. *Physica Medica* 26 (2),
321 88–97.